



Ehlers-Danlos syndrome in a dog

Rafael Barrera, Cinta Mañe, Esther Duran, Miguel A. Vives, Concepcion Zaragoza

A 7-month-old, female Alaskan malamute, weighing 29.6 kg, was presented to the Veterinary Teaching Hospital (VTH), University of Extremadura (Spain), for further evaluation of skin wounds of unknown etiology and a history of cutaneous lesions from birth. The dog had been treated previously on 4 occasions with antibiotics for gaping wounds with no apparent cause.

On clinical examination, the dog showed 2 "fish mouth" wounds in the right hind limb and neck that showed well-defined limits and a small amount of hemorrhage. The lacerations had appeared 3 and 1 d earlier, respectively, neither appeared to be painful or infected.

The skin could be stretched to extreme lengths (Figure 1), and no signs referable to the locomotor or other systems were noticed. The rectal temperature was 37.2°C and the routine hematological tests showed mild leukocytosis as the only apparent abnormality (18.1×10^9 cells/L; reference range, 7.5 to 15.06×10^9 L). Results from microbiological culture of skin samples from the wounds were negative. Empiric treatment based in wound cleaning and topical administration of a gauze embedded with neomycin sulfate, polymyxin B sulfate, and bacitracin ointment was recommended.

On day 26, the dog was reinspected at the VTH and showed a fresh wound on the right forelimb. The earlier lacerations had healed readily, but they had left thin and highly visible "cigarette paper" scars. The fresh wound had a similar appearance to the previous lacerations, although there were some signs of inflammation. Hematological tests revealed once more the existence of mild leukocytosis (20.4×10^9 cells/L) and skin samples were obtained again for a microbiological culture. *Pseudomonas* spp, susceptible to marbofloxacin (+++), norfloxacin (+++), trimethoprim-sulfamethoxazole (+++), tetracycline (+), and gentamicin (+), were obtained. Resistance to penicillin G and erythromycin was noticed. The degree of skin hyperextensibility was evaluated by means of the skin extensibility index devised by Patterson and Minor for the cat (1) (skin extensibility index = length of elbow skinfold [tuber olecrani-tip skin] $\times 100$ versus the length of the dog). The index obtained in this animal was 19.1. A skin biopsy was taken, fixed in 10% formalin, and prepared for histopathological examination: The epidermis and dermis surrounding the wound site showed thinning and



Figure 1. Hyperextensibility of the skin is demonstrated.

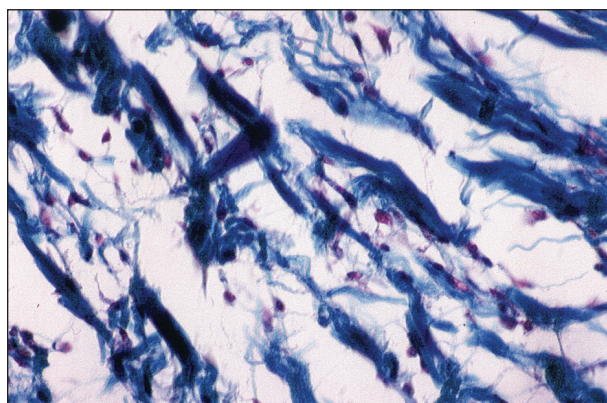


Figure 2. Detail of a collagen bundle showing reddish color (Masson's trichrome stain, 40 \times).

orthokeratotic hyperkeratosis. The epidermis showed disorganization, and eosinophilic infiltrate with presence of cellular debris. Dermal collagen fibers formed irregularly sized bundles; both fibers and bundles showed fragmentation and disorientation. In samples stained with Masson's trichrome (Figure 2), some collagen fibers were red. Spongiform microabscess formation over the wound site was also noticed. A moderate number of mononuclear inflammatory cells were observed throughout the middle and lower dermis.

The history and clinical findings were consistent with Ehlers-Danlos syndrome. Symptomatic treatment included providing a protected environment; the administration of marbofloxacin (Marbocyl; Vétoquinol, Paris, France), 2 mg/kg bodyweight (BW), PO, q24h, and vitamin C, 500 mg, PO, q12h; wound cleansing; and the topical administration of neomycin sulfate, polymyxin B sulfate, and bacitracin ointment. The

Departamento de Medicina y Sanidad Animal, Universidad de Extremadura, Facultad de Veterinaria, Avda. Universidad s/n, 10004 Caceres, Spain.

Address all correspondence and reprint requests to Dr. Concepcion Zaragoza; e-mail: zaragoza@unex.es

owner was informed of the nature, heritability, and chronic, incurable course of the disease, and advised not to use the dog for breeding.

Ehlers-Danlos syndrome is included in a group of inherited connective tissue diseases characterized by skin fragility, skin hyperextensibility, joint hypermobility, and vascular fragility (2). The terms "cutaneous asthenia" and "dermatosparaxis" are also used to describe this disease. In human medicine, cutaneous asthenia is reserved for cases wherein some abnormalities in both collagen and elastin (cutis laxa) exist, although such cases have not been definitively documented in animals. The term "dermatosparaxis" is used to describe 1 specific type (VIIC) of Ehlers-Danlos syndrome. The patients with this subtype are characterized mainly by showing high skin fragility (3).

The Ehlers-Danlos syndrome has been reported in sheep, cattle, mink, dogs, and cats (4–6). It is a rare skin disease in the dog, although several cases have been reported and in various breeds: German shepherd dog, beagle, dachshund, English springer spaniel, boxer, St. Bernard, soft-coated wheaten terrier, Garafiano shepherd, Fila brasileiro, greyhound, Manchester terrier, Welsh corgi, red kelpi, Irish setter, keeshond, toy poodle, English setter, Yorkshire terrier, and mongrels (2–4,6–8). However, this list of potentially affected breeds is of little value, because every new publication adds a new breed to the list. Diagnosis may be difficult because several subtypes of the disorder have been reported. In humans, 10 subtypes, based on the clinical features, mode of inheritance, and nature of the biochemical defect, are defined (8); not all cases in dogs can be categorized in this scheme. Ehlers-Danlos syndrome is usually diagnosed in young animals (2), although, Freeman et al (8) reported this disorder in 3 dogs from 6 to 8 y of age.

A characteristic of this disease is a fragile and hyperextensibility of skin, which may be used to differentiate this disorder from some other acquired diseases (5). The tensile strength of the skin has been reported as being reduced by 40-fold in affected dogs (9); therefore, the skin extensibility index may be useful as a simple aid in evaluating and diagnosing the disease. In affected dogs, the parameter is > 14.5 (1).

Because of the collagen defects, the skin often tears easily in affected dogs, resulting in large, crapping "fish mouth" wounds (7). Although delayed wound healing is

frequently mentioned as a complication in humans with Ehlers-Danlos syndrome (10), the wounds in this case healed readily. In addition, the wounds were characterized by low bleeding (2). Also, other signs of the disease, like subcutaneous hematomas at sites of injury, joint laxity, and ocular signs (7), were not observed in this dog.

Hematological evaluation failed to reveal any abnormalities other than a mild neutrophilia, as a result of inflammation and infection of cutaneous wounds. The diagnosis can be made clinically, based in history and clinical examination, and confirmed histopathologically with the disorganization, disorientation, and fragmentation of the dermal collagen fibers.

Ehlers-Danlos syndrome should always be suspected when a young dog is presented with hyperextensibility of the skin and wounds not related to traumas. Although the prognosis must be considered as unfavorable, a protected environment and life-long treatment of the wounds can be established. In fact, the case described in this report has been treated for 2 y and, to date, no severe complications have been observed.

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